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 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  FEB 25   CA/CAPLUS - Russian Agency for Patents and Trademarks
                   (ROSPATENT) added to list of core patent offices covered
 NEWS  4  FEB 28   PATDPAFULL - New display fields provide for legal status
                   data from INPADOC
 NEWS  5  FEB 28   BABS - Current-awareness alerts (SDIs) available
 NEWS  6  FEB 28   MEDLINE/LMEDLINE reloaded
 NEWS  7  MAR 02   GBFULL: New full-text patent database on STN
 NEWS  8  MAR 03   REGISTRY/ZREGISTRY - Sequence annotations enhanced
 NEWS  9  MAR 03   MEDLINE file segment of TOXCENTER reloaded
 NEWS  10 MAR 22   KOREAPAT now updated monthly; patent information enhanced
 NEWS  11 MAR 22   Original IDE display format returns to REGISTRY/ZREGISTRY
 NEWS  12 MAR 22   PATDPASPC - New patent database available
 NEWS  13 MAR 22   REGISTRY/ZREGISTRY enhanced with experimental property tags
 NEWS  14 APR 04   EPFULL enhanced with additional patent information and new
                   fields
 NEWS  15 APR 04   EMBASE - Database reloaded and enhanced
 NEWS  16 APR 18   New CAS Information Use Policies available online

 NEWS EXPRESS  JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

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FILE 'MEDLINE' ENTERED AT 11:15:49 ON 21 APR 2005

FILE 'BIOSIS' ENTERED AT 11:15:49 ON 21 APR 2005

=> s peptide and space filling
L1 58 PEPTIDE AND SPACE FILLING

=> s l1 and py<1999
L2 48 L1 AND PY<1999

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L3 33 DUPLICATE REMOVE L2 (15 DUPLICATES REMOVED)

=> d 1-10 bib ab

L3 ANSWER 1 OF 33 MEDLINE on STN DUPLICATE 1
AN 1998118527 MEDLINE
DN PubMed ID: 9443945
TI Steric hindrance mutagenesis versus alanine scan in mapping of ligand binding sites in the tachykinin NK1 receptor.
AU Holst B; Zoffmann S; Elling C E; Hjorth S A; Schwartz T W
CS Laboratory for Molecular Pharmacology, University of Copenhagen, Rigshospitalet, Denmark.
SO Molecular pharmacology, **(1998 Jan)** 53 (1) 166-75.
Journal code: 0035623. ISSN: 0026-895X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199802
ED Entered STN: 19980306
Last Updated on STN: 19980306
Entered Medline: 19980220
AB Residues in transmembrane domain (TM)-III, TM-V, TM-VI, and TM-VII believed to be facing the deep part of the presumed main ligand-binding pocket of the NK1 receptor were probed by alanine substitution and introduction of residues with larger and/or chemically distinct side chains. Unaltered or even improved binding affinity for four **peptide** agonists, substance P, substance P-O-methyl ester, eledoisin, and neurokinin A, as well as normal EC50 values for substance P in stimulating phosphatidylinositol turnover indicated that these mutations did not alter the overall functional integrity of the receptor. The alanine substitutions in general had only minor effects on nonpeptide antagonist binding. However, the introduction of the larger and polar aspartic acid and histidine residues at positions corresponding to the monoamine binding aspartic acid in TM-III of the beta 2-adrenoceptor (ProIII:08, Pro112 in the NK1 receptor) and to the presumed monoamine interacting "two serines" in TM-V (ThrV:09, Thr201; and IleV:12, Ile204) impaired by > 100-fold the binding of a group of nonpeptide antagonists, including CP96,345, CP99,994, RP67,580, RPR100,893, and CAM4092. In contrast, another group of nonpeptide antagonists, LY303,870, FK888, and SR140,333, were little or not at all affected by the **space-filling** substitutions. Two of these compounds, FK888 and LY303,870, were those most seriously affected (75-89-fold) by alanine substitution of PheVI:20 located in the upper part of the main ligand-binding crevice. Surprisingly, substitution of AlaIII:11 (Ala115), which is located in the middle of TM-III, conceivably pointing toward TM-VII, with a larger valine residue increased the affinity for all 13 ligands tested, presumably by creating a closer interhelical packing. It is concluded that the introduction of larger side chains at positions at

which molecular models indicate that this is structurally allowed can be a powerful method of locating ligand-binding sites due to the considerable difference between positive and negative results. Such steric hindrance mutagenesis strongly indicates that one population of nonpeptide antagonists bind in the deep pocket of the main ligand-binding crevice of the NK1 receptor, whereas another group of nonpeptide antagonists, especially SR140,333, was surprisingly resistant to mutational mapping in this pocket.

L3 ANSWER 2 OF 33 MEDLINE on STN DUPLICATE 2
AN 97350842 MEDLINE
DN PubMed ID: 9207218
TI Beta-helical fibrils from a model **peptide**.
AU Lazo N D; Downing D T
CS Department of Dermatology, The University of Iowa College of Medicine, Iowa City 52242, USA.. nlazo@blue.weeg.uiowa.edu
NC AR32374 (NIAMS)
SO Biochemical and biophysical research communications, **(1997 Jun 27)** 235 (3) 675-9.
Journal code: 0372516. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199707
ED Entered STN: 19970805
Last Updated on STN: 19970805
Entered Medline: 19970724
AB A synthetic **peptide**, KLEG13 (Ac-KLKLKLELELELG-NH2), composed of alternating bulky hydrophilic and hydrophobic amino acid residues formed clear, viscous dispersions of fibrils in saline solutions. The fibrils had a uniform diameter of 2 nm as measured on electron micrographs of negatively stained preparations. 13C solid-state nuclear magnetic resonance spectroscopy of the fibrils indicated the presence of a beta-conformation. Circular dichroic spectra of the dispersion of fibrils were essentially identical to the calculated spectrum of a 100% beta-helix. **Space-filling** CPK models of a proposed beta-helical conformation of the **peptide**, in which the leucine side chains form a hydrophobic core and the hydrophilic lysine and glutamate side chains extend outwards from the helix, had a diameter consistent with the observed 2-nm diameter of the fibrils. This study may have implications regarding the structure of amyloid fibrils.

L3 ANSWER 3 OF 33 MEDLINE on STN
AN 1998051701 MEDLINE
DN PubMed ID: 9390262
TI Statistical geometry analysis of proteins: implications for inverted structure prediction.
AU Tropsha A; Singh R K; Vaisman I I; Zheng W
CS Laboratory for Molecular Modeling, University of North Carolina at Chapel Hill, NC 27599, USA.
SO Pacific Symposium on Biocomputing. Pacific Symposium on Biocomputing, **(1996)** 614-23.
Journal code: 9711271.
CY Singapore
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199801
ED Entered STN: 19980122
Last Updated on STN: 19980122
Entered Medline: 19980108
AB The topology of folded proteins from the representative dataset of well-defined three-dimensional protein structures is studied using a

statistical geometry approach. Amino acid residues in protein chains are represented by C alpha atoms, thus reducing the protein three-dimensional structure to a set of points in three dimensional space. The Delaunay tessellation of a protein structure generates an aggregate of **space-filling** irregular tetrahedra, or Delaunay simplices. Each simplex objectively defines four nearest neighbor C alpha atoms, i.e. four nearest neighbor residues. The statistical analysis of residue composition of Delaunay simplices reveals nonrandom preferences for certain quadruplets of amino acids. These nonrandom preferences are used to develop a fitness function that evaluates sequence-structure compatibility. Using this fitness function, several tested native proteins score the highest among 100,000 random sequences with average protein amino acid composition. The statistical geometry approach, based solely on first principles, provides a unique means for protein structure analysis and has direct implications for inverted protein structure prediction.

L3 ANSWER 4 OF 33 MEDLINE on STN DUPLICATE 3
AN 96298235 MEDLINE
DN PubMed ID: 8679946
TI Topographic analysis of the S7 binding subsite of the tachykinin neurokinin-1 receptor.
AU Josien H; Convert O; Berlose J P; Sagan S; Brunissen A; Lavielle S; Chassaing G
CS Laboratoire de Chimie, Organique Biologique, CNRS URA 493, Universite Pierre et Marie Curie, Paris, France.
SO Biopolymers, **(1996 Aug)** 39 (2) 133-47.
Journal code: 0372525. ISSN: 0006-3525.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199608
ED Entered STN: 19960828
Last Updated on STN: 19960828
Entered Medline: 19960821
AB Conformationally and configurationally restricted rotameric probes of phenylalanine have been incorporated in the sequence of substance P (SP)-Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Gly-Leu-Met-NH2-for analyzing the binding pockets of Phe7 (S7) and Phe8 (S8), in the neurokinin-1 receptor. These analogues of phenylalanine are (2S. 3R)- and (2S, 3S)-indanylglycines, E- and Z-alpha, beta-dehydrophenylalanines, and 2(S)-alpha, beta-cyclopropylphenylalanines [delta E Phe. delta Z Phe. inverted delta E2 (S) Phe, and inverted delta Z 2 (S) Phe]. Binding data obtained with either conformationally (Ing diastereoisomers) or configurationally (delta E Phe, delta Z Phe) probes have unveiled large differences in the binding potencies of these rotameric probes. With the support of nmr data and energy calculations done on these SP-substituted analogues, we attempt to answer questions inherent to such study. First, none of these six probes prevents the formation of bioactive conformation(s) of the backbone of SP. Second, both diastereoisomers (S, S) and (S, R) of indanylglycine preferentially adopt, in the sequence of SP, the gauche (-) and trans side-chain orientations, respectively, as previously postulated from energy calculations with model **peptides** . However, in solution, the difference in energy between these rotamers included in the sequence of SP, compared to model **peptides**, is small since the other rotamer can be detected in [(2S, 3R)Ing7]SP. Finally, from this study we can hypothesize that the large variations observed in the affinities of Phe7 substituted analogues of SP must come from steric hindrance in the S7 binding site, which drastically restricts the **space filling** around the C alpha-C beta bond of residue 7.

L3 ANSWER 5 OF 33 MEDLINE on STN DUPLICATE 4

AN 95346408 MEDLINE
DN PubMed ID: 7620985
TI PBM: a software package to create, display and manipulate interactively models of small molecules and proteins on IBM-compatible PCs.
AU Perrakis A; Constantinides C; Athanasiades A; Hamodrakas S J
CS Department of Biochemistry, Cell and Molecular Biology and Genetics, University of Athens, Greece.
SO Computer applications in the biosciences : CABIOS, **(1995 Apr)** 11 (2) 141-5.
Journal code: 8511758. ISSN: 0266-7061.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199508
ED Entered STN: 19950911
Last Updated on STN: 19950911
Entered Medline: 19950831
AB The PBM package was developed to create, display and conveniently manipulate protein and small molecule structures on IBM-compatible microcomputers. It consists of four modules: CREATE, SPHERE, RIBBON and CONVERT. CREATE includes commands to create or alter ('mutate') the primary and subsequently the tertiary structure of a given **peptide** or protein by defining phi and psi angles of residues at will, options to add, delete or alter atoms in a structure, utilities to choose easily between the most common rotamers of amino acid residue sidechains and options to analyse in various ways a protein conformation. SPHERE provides for an interactive manipulation of structures containing up to 2700 atoms which can belong up to six different molecules. All manipulations can be made with the use of an ordinary mouse, by choosing from a variety of pull-down menus. Three types of models can be implemented to display molecules on the computer screen or the plotter: skeletal, solid **space-filling** and wireframe **space-filling** models. RIBBON creates ribbon models of proteins and allows for a limited variety of interactive manipulations. CONVERT is a file converter, which is capable of converting files of atom coordinates of literally any format to Brookhaven Data Bank format files. The package produces very good results for protein molecules of reasonable sizes, both in terms of graphics quality and speed of operations, on an 80486 IBM PC-compatible machine equipped with a 1 MByte VGA display card and a colour VGA monitor, which is a recommended configuration.

L3 ANSWER 6 OF 33 MEDLINE on STN
AN 95118954 MEDLINE
DN PubMed ID: 7819165
TI MacMolecular: a program for visualization of molecular structures on the Macintosh.
AU Weaver T D; Islam S A; Weaver D L
CS Dartmouth College, Hanover, NH.
SO Journal of molecular graphics, **(1994 Sep)** 12 (3) 231-4, 200.
Journal code: 9014762. ISSN: 0263-7855.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199502
ED Entered STN: 19950223
Last Updated on STN: 20000303
Entered Medline: 19950216
AB MacMolecular displays small- to medium-sized biomolecules, with particular emphasis on **peptides**. It has been developed to run on color Macintosh computers. The display can be stick, ball and stick, depth cued by thickness stick, or several types of **space-filling** representations. The program takes input from standard PDB files, simple

Cartesian coordinate files, and, in addition, from Kinemage files in which atom information has been included. The program allows color changes of various types as well as the normal functions of translation, rotation, and zooming. In addition, animation files may be produced for subsequent display. Bonding of atoms is done by a distance algorithm (standard) or sequentially to properly display C alpha traces and traces of **peptides** containing simplified representations of amino acids. Stereo viewing is available, and manipulated structures which were drawn from PDB files can be written out to new PDB files. In addition, PICT files of the drawing window can be generated.

L3 ANSWER 7 OF 33 MEDLINE on STN
AN 93272924 MEDLINE
DN PubMed ID: 8500595
TI The link proteins.
AU Neame P J; Barry F P
CS Shriners Hospital for Crippled Children, Tampa, Florida.
NC AR 35322 (NIAMS)
SO Experientia, **(1993 May 15)** 49 (5) 393-402. Ref: 77
Journal code: 0376547. ISSN: 0014-4754.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 199306
ED Entered STN: 19930716
Last Updated on STN: 19990129
Entered Medline: 19930629
AB Aggregates of chondroitin-keratan sulfate proteoglycan (aggrecan) and hyaluronic acid (hyaluronan) are the major **space-filling** components of cartilage. A glycoprotein, link protein (LP; 40-48 kDa) stabilizes the aggregate by binding to both hyaluronic acid and aggrecan. In the absence of LP, aggregates are smaller (as estimated by rotary shadowing of electron micrographs) and less stable (they dissociate at pH 5) than they are in the presence of LP. The proteoglycan aggregate, including LP, is dissociated in the presence of chaotropes such as 4 M guanidine hydrochloride. On removal of the chaotrope, the complex will reassociate. This forms the basis of the isolation of LP from cartilage and has been described in detail elsewhere. Tryptic digestion of the proteoglycan aggregates results in a high molecular weight product that consists of hyaluronic acid to which is bound LP and the N-terminal globular domain of aggrecan (hyaluronic acid binding region; HABR) in a 1:1 stoichiometry. The amino acid sequences of LP and HABR are surprisingly similar. The amino acid sequence can be divided into three domains; an N-terminal domain that falls into the immunoglobulin super-family and two C-terminal domains that are similar to each other. The DNA structure echoes this similarity, in that the major domains are reflected in three separate exons in both LP and HABR. The two C-terminal domains are largely responsible for the association with HA and are related to two recently described hyaluronate-binding proteins, CD44 and TSG-6. A variety of approaches, including analysis of the forms of LP found in vivo, rotary shadowing and analysis of the sequence in the immunoglobulin-like domain, have shed considerable light on the structure-function relationships of LP. This review describes the structure and function of LP in detail, focusing on what can be inferred from the similarity of LP, HABR and related molecules such as immunoglobulins and lymphocyte HA-receptors.

L3 ANSWER 8 OF 33 MEDLINE on STN DUPLICATE 5
AN 93056535 MEDLINE
DN PubMed ID: 1431130
TI Biochemical specificity of H-2M3a. Stereospecificity and **space-filling** requirements at position 1 maintain N-formyl

peptide binding.
AU Vyas J M; Shawar S M; Rodgers J R; Cook R G; Rich R R
CS Department of Microbiology and Immunology, Baylor College of Medicine, Houston, TX 77030.
NC AI18882 (NIAID)
SO Journal of immunology (Baltimore, Md. : 1950), **(1992 Dec 1)** 149 (11) 3605-11.
Journal code: 2985117R. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199212
ED Entered STN: 19930122
Last Updated on STN: 20020724
Entered Medline: 19921221
AB The maternally transmitted Ag is a cell surface product of three gene products: 1) H-2M3a (formerly Hmta), a class I MHC heavy chain; 2) beta 2-microglobulin; and 3) maternally transmitted factor (Mtf), the N-terminus of the mitochondrially encoded ND1 subunit of the reduced form of nicotinamide-adenine dinucleotide dehydrogenase. This class I molecule has been shown to be an N-formyl **peptide** receptor. Although the N-formyl moiety is necessary for binding to M3a, it is not sufficient. We proposed that the R group of the amino acid in position 1 plays a pivotal role in **peptide** binding to M3a. To test this hypothesis, analogues differing in size and stereospecificity of the R group were synthesized. Substitutions with other hydrophobic amino acids such as N-formyl phenylalanine and N-formyl valine had no significant effect on the ability of these Mtf alpha analogues to sensitize target cells (M3a, Mtf beta) to M3a, Mtf alpha-specific CTL. In contrast, the nonsubstituted, N-formylated, and N-acetylated glycyl analogues of Mtf beta bound equivalently to M3a in a **peptide** competition assay. Moreover, the alanine analogue bound in an N-formyl-dependent manner. To determine the limitations of the putative N-formyl pocket, **peptide** analogues were constructed incorporating D-isomer amino acids. When formylated D-alanine or D-methionine replaced the native methionine, these **peptide** derivatives did not show significant binding to M3a. Therefore, the presence of a **space-filling** R group (greater than hydrogen) is necessary for an antigenic **peptide** to bind M3a in an N-formyl-dependent manner. Additionally, the ability of M3a to discriminate between the optical forms of methionine and alanine demonstrates that this N-formyl pocket is stereospecific in its ability to bind **peptide**. Thus, we have defined three requirements for **peptide** binding to M3a: an N-formyl moiety at the amino terminus of the **peptide**, a **space-filling** R group at position 1 to maintain this N-formyl specificity, and the correct stereoisomer of the first amino acid.

L3 ANSWER 9 OF 33 MEDLINE on STN DUPLICATE 6
AN 91331975 MEDLINE
DN PubMed ID: 1869515
TI Evidence for the presence of a specific ganglioside GM1/valinomycin complex in mixed monolayers.
AU Schifferer F; Cordroch W; Beitinger H; Mobius D; Rahmann H
CS Zoological Institute, Universitat Stuttgart-Hohenheim, F.R.G.
SO Journal of biochemistry, **(1991 Apr)** 109 (4) 622-6.
Journal code: 0376600. ISSN: 0021-924X.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199109
ED Entered STN: 19911006
Last Updated on STN: 19911006

Entered Medline: 19910917

AB The effect of a negatively charged mono-sialoglyco-sphingolipid (GM1-ganglioside) on the molecular organization and on physiochemical properties of lipid/**peptide** (valinomycin) systems was investigated in monolayers at the air/water interface. At a high molar fraction of GM1, the surface pressure/area isotherms of the two-component films of the system GM1/valinomycin and the isotherm of the pure ganglioside monolayer are identical concerning the space requirement of the molecules and thereby the packing of the monolayer. Using **space-filling** molecular models, a simple calculation gives the theoretical amount of 4.5 ganglioside molecules associated with one molecule of the depsipeptide valinomycin. The average surface potential indicates, that valinomycin, interacting with the polar head group of GM1, becomes partly embedded within the lipid interface. For GM1/eicosanol and valinomycin/eicosanol mixtures, the agreement between theory and experimental data strongly supports the model of ideal mixing without any molecular interactions between the different components. The results suggest the formation of a ganglioside/valinomycin complex with simultaneous alteration of the surface potential and molecular structure of the single components.

L3 ANSWER 10 OF 33 MEDLINE on STN
AN 89005917 MEDLINE
DN PubMed ID: 2458979
TI Molecular defects in ion channel regulation in cystic fibrosis predicted from analysis of protein phosphorylation/dephosphorylation.
AU Brautigan D L
CS Division of Biology and Medicine, Brown University, Providence, RI 02912.
NC DK31374 (NIDDK)
SO International journal of biochemistry, **(1988)** 20 (8) 745-52.
Ref: 20
Journal code: 0250365. ISSN: 0020-711X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 198811
ED Entered STN: 19900308
Last Updated on STN: 19970203
Entered Medline: 19881115

AB 1. Recent discoveries have implicated regulation of an apical membrane chloride channel as site of a defect in cystic fibrosis (CF). The channel fails to respond to stimuli that elevate intracellular cAMP. 2. This paper describes properties of reversible cycles of protein phosphorylation and considers substrate specificity, reactions with model **peptides** , and **space-filling** structural models. 3. Mutation of a channel regulatory protein is proposed to involve either: (a) change of phosphorylated serine residue to an unreactive residue, (b) change in a nearby residue that does not affect phosphorylation by cAMP-dependent kinase, but results in dephosphorylation by a different phosphatase, or (c) change in a nearby residue that produces a structure unreactive with cAMP-dependent protein kinase. 4. Perhaps in CF sidechains with branched structures at the beta carbons occur on either side of the phosphorylated serine, like in glycogen phosphorylase, and prohibit reaction of a regulatory protein with cAMP-dependent protein kinase.

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                   (ROSPATENT) added to list of core patent offices covered
 NEWS  4  FEB 28   PATDPAFULL - New display fields provide for legal status
                   data from INPADOC
 NEWS  5  FEB 28   BABS - Current-awareness alerts (SDIs) available
 NEWS  6  FEB 28   MEDLINE/LMEDLINE reloaded
 NEWS  7  MAR 02   GBFULL: New full-text patent database on STN
 NEWS  8  MAR 03   REGISTRY/ZREGISTRY - Sequence annotations enhanced
 NEWS  9  MAR 03   MEDLINE file segment of TOXCENTER reloaded
 NEWS  10 MAR 22   KOREAPAT now updated monthly; patent information enhanced
 NEWS  11 MAR 22   Original IDE display format returns to REGISTRY/ZREGISTRY
 NEWS  12 MAR 22   PATDPASPC - New patent database available
 NEWS  13 MAR 22   REGISTRY/ZREGISTRY enhanced with experimental property tags
 NEWS  14 APR 04   EPFULL enhanced with additional patent information and new
                   fields
 NEWS  15 APR 04   EMBASE - Database reloaded and enhanced
 NEWS  16 APR 18   New CAS Information Use Policies available online

 NEWS EXPRESS  JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

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FULL ESTIMATED COST                                    0.21        0.21
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FILE 'MEDLINE' ENTERED AT 12:46:27 ON 21 APR 2005

FILE 'BIOSIS' ENTERED AT 12:46:27 ON 21 APR 2005

=> s pharmacophore and peptide
L1 573 PHARMACOPHORE AND PEPTIDE

=> s l1 and review/dt
L2 41 L1 AND REVIEW/DT

=> s l2 and py<1999
L3 13 L2 AND PY<1999

=> duplicate remove l3
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L4 13 DUPLICATE REMOVE L3 (0 DUPLICATES REMOVED)

=> d 1-13 bib ab

L4 ANSWER 1 OF 13 MEDLINE on STN
AN 97385411 MEDLINE
DN PubMed ID: 9241425
TI Bacteriophage display and discovery of **peptide** leads for drug development.
AU Lowman H B
CS Department of Protein Engineering, Genentech Inc, South San Francisco, California 94080, USA.. hbl@gene.com
SO Annual review of biophysics and biomolecular structure, **(1997)** 26 401-24. Ref: 67
Journal code: 9211097. ISSN: 1056-8700.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199709
ED Entered STN: 19970916
Last Updated on STN: 19970916
Entered Medline: 19970904
AB Phage display makes large-**peptide** diversity libraries readily attainable for identifying novel **peptide** ligands for receptors and other protein or non-protein targets. This technology kindles enthusiasm for the idea that large and protein-protein interaction surfaces (epitopes) can be distilled down to small **pharmacophores** . These may be accessible to organic scaffolding, yielding new orally active drugs that might otherwise have taken greater time and effort to be discovered through chemical-library screening. This review, though not comprehensive with respect to the explosive volume of phage display work over the last few years, focuses on recent developments in phage-displayed **peptide** technology.

L4 ANSWER 2 OF 13 MEDLINE on STN
AN 97435018 MEDLINE
DN PubMed ID: 9291241
TI Clinical pharmacology of eptifibatide.
AU Phillips D R; Scarborough R M
CS COR Therapeutics, Inc., South San Francisco, California 94080, USA.
SO American journal of cardiology, **(1997 Aug 18)** 80 (4A) 11B-20B.
Ref: 70
Journal code: 0207277. ISSN: 0002-9149.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199709
ED Entered STN: 19970926
Last Updated on STN: 19970926
Entered Medline: 19970918
AB Activation of receptor function of platelet membrane glycoprotein (GP) IIb-IIIa leads to the binding of fibrinogen and is the final common pathway to platelet aggregation. Platelet aggregates provide the structural basis for coronary thrombosis, a major cause of ischemic heart disease. GP IIb-IIIa has a narrow tissue distribution, being found only on platelets and their progenitors, and inhibition of its receptor function has emerged as a promising new therapeutic strategy for management of acute ischemic coronary syndromes and acute ischemic complications of percutaneous coronary interventions. Eptifibatide (INTEGRILIN) is a cyclic heptapeptide inhibitor of GP IIb-IIIa, with an active **pharmacophore** that is derived from the structure of barbourin, a GP IIb-IIIa inhibitor from the venom of the southeastern pigmy rattlesnake. Like barbourin, eptifibatide is a specific and robust inhibitor of the GP IIb-IIIa receptor function, having a low affinity for other integrins and strongly preventing platelet aggregation. Preclinical pharmacologic studies have established that eptifibatide can inhibit thrombosis effectively, with only modest effects on bleeding time measurements. Pharmacokinetic and pharmacodynamic studies in both animal models and humans have shown that the antiplatelet effect of eptifibatide has a rapid onset of action and that the drug has a short plasma half-life. Furthermore, the rapid reversibility of action of eptifibatide, exemplified by an antihemostatic effect limited to the period of drug administration, was apparent in both healthy volunteers and patients with ischemic heart disease. In clinical trials, eptifibatide has not been found to be immunogenic or to induce thrombocytopenia. These studies have led to the evaluation of eptifibatide in the pivotal Integrilin to Minimize Platelet Aggregation and Coronary Thrombosis (IMPACT II) trial, which enrolled 4,010 patients undergoing coronary angioplasty. The combination of a bolus plus either of 2 infusion doses of eptifibatide reduced the incidence of ischemic complications without increasing the risk of bleeding or other complications. Recent pharmacodynamic studies have established that more aggressive dosing of eptifibatide provides greater inhibition of ex vivo platelet aggregation and more robust antithrombotic activity. Higher doses of eptifibatide were therefore selected for the Platelet GP IIb-IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy (PURSUIT) trial, which enrolled patients with unstable angina or non-Q-wave myocardial infarction. The available data suggest that eptifibatide may represent a useful clinical alternative to existing antiplatelet therapies.

L4 ANSWER 3 OF 13 MEDLINE on STN
AN 97114631 MEDLINE
DN PubMed ID: 8956365
TI Rational design, analysis, and potential utility of GM-CSF antagonists.
AU Monfardini C; Kieber-Emmons T; VonFeldt J M; Godillot A P; Voet D; Weiner D B; Williams W V
CS Department of Medicine, University of Pennsylvania, Philadelphia 19103, USA.
SO Proceedings of the Association of American Physicians, **(1996 Nov)** 108 (6) 420-31. Ref: 55
Journal code: 9514310. ISSN: 1081-650X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English

FS Priority Journals
EM 199703
ED Entered STN: 19970321
Last Updated on STN: 19970321
Entered Medline: 19970312
AB Granulocyte-macrophage colony-stimulating factor (GM-CSF) is an important cytokine involved in many immune and inflammatory processes and is believed to act in the early stages of immune responses. GM-CSF stimulates antigen-presenting cells, enhancing antigen presentation and inducing macrophage tumoricidal activity. GM-CSF binds to specific cellular receptors that are potential targets for pharmacological design. Rational design of small-molecule mimics is an important approach to **pharmacophore** design. One of the strategies in the development of small-molecular mimics of larger polypeptyde ligands is analysis of alternative ligands that bind the same site as does the native ligand. Molecular studies of GM-CSF-receptor interactions have led to the development of interaction site analogs and the development of an "anti-anti-GM-CSF" recombinant antibody (rAb) analog of a site on GM-CSF important for biological activity and receptor binding. This rAb and a **peptide** derived from the rAb first complementarity determining region (CDR) sequence bind to a monoclonal anti-GM-CSF antibody that mimics the GM-CSFR alpha chain, compete with GM-CSF for binding to GM-CSF receptor alpha chain (GM-CSFR alpha), and are specific biological antagonists. Molecular modeling of the rAb suggests structural similarity with a site previously implicated in GM-CSF binding to the GM-CSFR alpha. Two cyclic **peptides**, 1785 and 1786, also were developed on the basis of structural analysis of the GM-CSF region mimicked by anti-anti-GM-CSF recombinant antibody (rAb) 23.2. These **peptides** were designed to mimic structurally the positions of specific residues on the B and C helicies of human GM-CSF implicated in receptor binding and bioactivity. Both 1785 and 1786 were recognized specifically by polyclonal anti-GM-CSF antibody. 1786 also competitively inhibited binding of GM-CSF to the GM-CSF receptor and demonstrated antagonist bioactivity, as shown by its reversal of GM-CSF's ability to inhibit apoptosis of the GM-CSF-dependent cell line MO7E. These studies support the role of residues on the GM-CSF B and C helicies in receptor binding and bioactivity and suggest strategies for mimicking binding sites on four-helix bundle proteins with cyclic **peptides**.

L4 ANSWER 4 OF 13 MEDLINE on STN
AN 97089252 MEDLINE
DN PubMed ID: 8935160
TI Chemical approaches to improve the oral bioavailability of peptidergic molecules.
AU Samanen J; Wilson G; Smith P L; Lee C P; Bondinell W; Ku T; Rhodes G; Nichols A
CS Department of Medicinal Chemistry, SmithKline Beecham Pharmaceuticals, King of Prussia, PA 19406, USA.
SO Journal of pharmacy and pharmacology, **(1996 Feb)** 48 (2) 119-35.
Ref: 68
Journal code: 0376363. ISSN: 0022-3573.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199612
ED Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961230
AB This review discusses both tools and strategies that may be employed as approaches towards the pursuit of orally active compounds from peptidergic molecules. Besides providing a review of these subjects, this paper

provides an example of how these were utilized in a research programme at SmithKline Beecham involving the development of orally active GPIIb/IIIa antagonists. The tools for studying oral drug absorption in-vitro include variants of the Ussing chamber which utilize either intestinal tissues or cultured epithelial cells that permit the measurement of intestinal permeability. Example absorption studies that are described are mannitol, cephalexin, the growth hormone-releasing **peptide** SK&F 110679 and two GPIIb/IIIa antagonist **peptides** SK&F 106760 and SK&F 107260. With the exception of cephalexin, these compounds cross the intestine by passive paracellular diffusion. Cephalexin, on the other hand, crosses the intestine via the oligopeptide transporter. Structure-transport studies are reviewed for this transporter. The tools for studying oral drug absorption in-vivo involve animals bearing in-dwelling intestinal or portal vein catheters. A study of the segmental absorption of SK&F 106760 is provided. The review concludes with two chemical strategies that may be taken towards the enhancement of oral bioavailability of peptidergic molecules. The first strategy involves the chemical modification of **peptides** which enhance intestinal permeability, specifically the modification of amide bonds. The second strategy involves the design of compounds bearing nonpeptide templates, which are more amenable to the discovery of compounds with oral activity, from **peptide pharmacophore** models. An example is given regarding the discovery of SB 208651, a potent orally active GPIIb/IIIa antagonist, designed from the **peptides** SK&F 106760 and SK&F 107260.

L4 ANSWER 5 OF 13 MEDLINE on STN
AN 97146985 MEDLINE
DN PubMed ID: 8993841
TI Molecular determinants of **peptide** and non-**peptide** binding to the AT1 receptor.
AU Karnik S S; Husain A; Graham R M
CS Department of Molecular Cardiology, Cleveland Clinic Foundation, Ohio 44195, USA.
NC HL33713 (NHLBI)
SO Clinical and experimental pharmacology & physiology. Supplement, **(1996)** 3 S58-66. Ref: 35
Journal code: 7611484. ISSN: 0143-9294.
CY Australia
DT Conference; Conference Article; (CONGRESSES)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199703
ED Entered STN: 19970407
Last Updated on STN: 20000303
Entered Medline: 19970326
AB 1. Several residues critically involved in AT1 receptor ligand-binding and activation have now been identified based on mutational and biochemical studies. 2. Asp281 and Lys199 of the rat AT1 receptor ion-pair with Arg2 and the Phe3 alpha-COOH of angiotensin II (AngII), respectively, and the Asp281/Arg2 interaction is critical for full agonist activity. 3. Agonist activity of AngII also requires an interaction of the Phe8 side chain with His256, which is achieved by docking of the alpha-COOH with Lys199. Non-**peptide** agonists interact with Lys199 and His256 in a similar fashion. 4. The crucial acid **pharmacophores** of AngII and the non-**peptide** antagonist, losartan, appear to occupy the same space within the receptor pocket. Binding of the tetrazole anion moiety of losartan involves multiple contacts, such as Lys199 and His256. However, this interaction does not involve a conventional salt bridge, but rather an unusual lysine-aromatic interaction. 5. Asp1 of AngII forms an ion-pair with His183, which stabilizes the receptor-bound conformation of AngII but is not critical for receptor activation. 6. These interactions and the involvement of

other residues in stabilizing the wild-type receptor conformation or in receptor/G-protein coupling are considered here. 7. Despite these insights, considerable effort is still needed to elucidate how ligand binding induces receptor activation, what determines the specificity of AT1 receptor coupling to multiple G-proteins and the in vivo role of receptor down-regulation.

L4 ANSWER 6 OF 13 MEDLINE on STN
AN 95308356 MEDLINE
DN PubMed ID: 7540497
TI Galanin--10 years with a neuroendocrine **peptide**.
AU Bedecs K; Berthold M; Bartfai T
CS Department of Neurochemistry and Neurotoxicology, Arrhenius Laboratories of Natural Sciences, Stockholm University, Sweden.
SO international journal of biochemistry & cell biology, **(1995 Apr)** 27 (4) 337-49. Ref: 120
Journal code: 9508482. ISSN: 1357-2725.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 199507
ED Entered STN: 19950807
Last Updated on STN: 19960129
Entered Medline: 19950721
AB Galanin is a 29/30 amino acids long neuropeptide which does not belong to any known **peptide** family. The N-terminal first 16 amino acids of the molecule are both necessary and sufficient for receptor recognition and receptor activation. The main **pharmacophores** of galanin in its central and pancreatic actions are Gly1, Trp2, Asn5 and Tyr9, respectively. The neuropeptide galanin has multiple effects in both the central and peripheral nervous systems. Centrally, galanin potently stimulates fat intake and impairs cognitive performance. Anoxic glutamate release in the hippocampus is inhibited by galanin and the noradrenergic tonus in the brain is influenced by a hyperpolarizing action of galanin in the locus coeruleus. In the spinal cord galanin inhibits spinal excitability and potentiates the analgesic effect of morphine. In the neuroendocrine system galanin acts in a stimulatory manner on the release of growth hormone and prolactin, and peripherally galanin inhibits glucose induced insulin release. Galanin also causes contraction of the jejunum. The galanin receptor is a Gi-protein-coupled, membrane-bound glycoprotein with an estimated molecular mass of 53 kDa. Several putative tissue specific galanin receptor subtypes have been proposed on a pharmacological basis. The distribution of galanin receptors and of galanin like immunoreactivity are overlapping in the CNS, both being high in areas such as the locus coeruleus, raphe nucleus and hypothalamus. Galanin receptor activation leads to a reduced intracellular Ca(2+)-concentration, either by direct action on voltage sensitive Ca(2+)-channels or indirectly via opening of K(+)-channels or via inhibition of adenylyl cyclase activity. The lowered intracellular Ca2+ level subsequently leads to a reduced PLC activity. Galanin also inhibits cGMP synthesis induced by depolarization. A number of synthetic high affinity galanin receptor antagonists of the **peptide** type were developed recently, which have enabled the elucidation of functional roles of endogenous galanin in several systems. Furthermore, putative subtypes of galanin receptors can be distinguished by the use of these new galanin receptor ligands.

L4 ANSWER 7 OF 13 MEDLINE on STN
AN 95201168 MEDLINE
DN PubMed ID: 7534489
TI Concept and progress in the development of RGD-containing **peptide** pharmaceuticals.
CM Erratum in: Biopolymers 1995;37(5):363

AU Craig W S; Cheng S; Mullen D G; Blevitt J; Pierschbacher M D
CS Telios Pharmaceutical, Inc., San Diego, California 92121.
SO Biopolymers, **(1995)** 37 (2) 157-75. Ref: 91
Journal code: 0372525. ISSN: 0006-3525.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 199504
ED Entered STN: 19950504
Last Updated on STN: 19960129
Entered Medline: 19950427
AB The cell adhesion domain, arginine-glycine-aspartic acid (RGD), has been incorporated into synthetic **peptides** to perform either of two modes of drug action, antagonist or agonist. Short, conformationally constrained **peptides** have been developed as antagonists for the platelet membrane glycoprotein complex, the integrin alpha IIb beta 3, using cell-based and integrin-based assays. In combination with a comparative molecular modeling study, these results have helped identify common conformational elements in the **pharmacophore** of this class of molecules. **Peptides** are presented that are highly potent, integrin specific, and that possess reduced pharmacological side effects. Also presented is the development of a **peptide** that modifies, noncovalently, the surfaces of a wide variety of synthetic materials used in medical implants. The agonist activity of [corrected] this molecule is evident from its ability to stimulate cell attachment on these surfaces. This is shown to translate into an in vivo activity of faster and more complete tissue integration, and a reduction in foreign body response.

L4 ANSWER 8 OF 13 MEDLINE on STN
AN 95201169 MEDLINE
DN PubMed ID: 7893947
TI Design and development of a vasoactive intestinal **peptide** analog as a novel therapeutic for bronchial asthma.
AU Bolin D R; Michalewsky J; Wasserman M A; O'Donnell M
CS Roche Research Center, Hoffmann-La Roche, Inc., Nutley, New Jersey 07110.
SO Biopolymers, **(1995)** 37 (2) 57-66. Ref: 43
Journal code: 0372525. ISSN: 0006-3525.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199504
ED Entered STN: 19950504
Last Updated on STN: 19950504
Entered Medline: 19950427
AB Analogs of vasoactive intestinal **peptide** (VIP) were synthesized and screened as bronchodilators with the ultimate goal of enhancing the potency and extending the duration of action of the native **peptide**. Several design approaches were applied to the problem. First, the amino acid residues required for receptor binding and activation were identified. A model of the active **pharmacophore** was developed. With knowledge of the secondary structure (NMR) of the **peptide**, various analogs were synthesized to stabilize alpha-helical conformations. Having achieved a level of enhanced bronchodilator potency, our approach then concentrated on identification of the sites of proteolytic degradation and synthesis of metabolically-stable analogs. Two primary cleavage sites on the VIP molecule were identified as the amide bonds between Ser25-Ile26 and Thr7-Asp8. This information was used to synthesize cyclic **peptides** which incorporated disulfide and

lactam ring structures. Analog work combined the best multiple-substitution sites with potent cyclic compounds which resulted in identification of a cyclic lead **peptide**. This compound, Ro 25-1553, exhibited exceptionally high potency, metabolic stability, and a long duration of action and may be an effective therapeutic for the treatment of bronchospastic diseases.

L4 ANSWER 9 OF 13 MEDLINE on STN
AN 94170754 MEDLINE
DN PubMed ID: 8125070
TI An overview of gastrointestinal endocrine physiology.
AU Brown J C
CS Department of Physiology, University of British Columbia, Vancouver, Canada.
SO Endocrinology and metabolism clinics of North America, **(1993 Dec)** 22 (4) 719-29. Ref: 68
Journal code: 8800104. ISSN: 0889-8529.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199404
ED Entered STN: 19940420
Last Updated on STN: 19940420
Entered Medline: 19940408
AB The biologic actions of the **peptides** of the gastrointestinal tract indicate that they exert their effects by interacting with, in many instances, more than one receptor type and receptors on several tissues. Gut hormone profiles in pathophysiologic situations have not demonstrated a significant role for them in disease states, other than in endocrine tumors of the gastroenteropancreatic system. The successful identification and subsequent cloning of the receptors to the regulatory **peptides**, knowledge of the control of their expression, and distribution will provide new insights into their possible involvement in pathophysiologic situations. Identification of **pharmacophores** from which to develop analogues, both agonists and antagonists, will provide powerful tools and potential therapeutic agents to expand knowledge in this field.

L4 ANSWER 10 OF 13 MEDLINE on STN
AN 94119186 MEDLINE
DN PubMed ID: 8289889
TI Computer design of bioactive compounds based on 3-D properties of ligands.
AU Martin Y C
CS Computer-Assisted Molecular Design Project, Abbott Laboratories, Abbott Park, IL 60064.
SO NIDA research monograph, **(1993)** 134 84-102. Ref: 28
Journal code: 8811762. ISSN: 1046-9516.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199402
ED Entered STN: 19940312
Last Updated on STN: 19940312
Entered Medline: 19940218
AB 3-D database searching has many uses for a medicinal chemist. It can aid in the design of compounds to probe or to mimic the bioactive conformation of a natural ligand or to fit a hypothetical or experimental structure of a binding site. It also can identify existing molecules that meet these

criteria--new uses for old molecules. If one has a database of active compounds, 3-D searching can validate or refute a **pharmacophore** hypothesis. The CoMFA method of 3DQSAR can be used to forecast the potency of the designed analogs. Also, the integration of CoMFA and 3-D searching concepts provides a framework for the design of a good series for CoMFA. In addition, CoMFA 3DQSAR coefficients provide a model of the binding site to facilitate the design of compounds that fit the **pharmacophore** and do not hit sterically unfavorable regions.

L4 ANSWER 11 OF 13 MEDLINE on STN
AN 93242665 MEDLINE
DN PubMed ID: 8480375
TI Endothelins--from receptors to medicine.
AU Miller R C; Pelton J T; Huggins J P
CS Marion Merrell Dow Research Institute, Strasbourg, France.
SO Trends in pharmacological sciences, **(1993 Feb)** 14 (2) 54-60.
Ref: 40
Journal code: 7906158. ISSN: 0165-6147.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199305
ED Entered STN: 19930611
Last Updated on STN: 19930611
Entered Medline: 19930524
AB Since the discovery of endothelins, **peptides** with exceptional vasoconstrictor potency that were originally suggested to act by causing the opening of Ca2+ channels, it has emerged that these agents are important in intercellular communication in many tissues. They exert their effects through G protein-coupled receptors, of which two classes have been cloned. Robert Miller, John Pelton and John Huggins review the progress made towards a molecular understanding of ligand recognition by endothelin receptors. Receptor-selective agonists and antagonists have emerged from attempts to understand the three-dimensional structure of the endothelin **pharmacophore**, from structure-activity studies and from rapid-screening programmes. From the nature of the secretion and action of endothelins, it would seem that these **peptides** are involved in long-term changes rather than in acute responses to stimuli, and that they are likely to be important in a number of pathological states. Evidence suggests that receptor antagonists with appropriate affinity and selectivity may be useful in the treatment of conditions as diverse as hypertension, ulcerogenesis and ciclosporin toxicity.

L4 ANSWER 12 OF 13 MEDLINE on STN
AN 93251934 MEDLINE
DN PubMed ID: 1302179
TI Useful functions of microbial metabolites.
AU Nisbet L J
CS Xenova Limited, Slough, Berks, UK.
SO Ciba Foundation symposium, **(1992)** 171 215-25; discussion 225-35.
Ref: 10
Journal code: 0356636. ISSN: 0300-5208.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199306
ED Entered STN: 19930618
Last Updated on STN: 19930618

Entered Medline: 19930609

AB The mood-enhancing effects of fungi and their medicinal properties have been recognized for centuries. Ergot was initially used by midwives to speed childbirth in the Middle Ages. More recently their pharmacological action on dopamine receptors has been exploited to treat post-partum bleeding, migraine, Parkinson's disease and senile dementia. Further indications of the potential value of microbial metabolites are exemplified by the discovery and development of cyclosporin, to treat organ rejection, and mevinolin, a cholesterol-lowering drug. Such discoveries are not unexpected because we have known for some time that fungi regulate morphogenesis, differentiation and sexuality via hormonal molecules, ranging from **peptides** through to steroidal molecules similar in structure to human sex hormones. A combination of the power of molecular biology to design screens based on isolated disease mechanisms with the chemical inventiveness of microorganisms is providing numerous new **pharmacophores** for drug development.

L4 ANSWER 13 OF 13 MEDLINE on STN
AN 89145113 MEDLINE
DN PubMed ID: 2852366
TI Cooperative reinforcement of opioid **pharmacophores**.
AU Lipkowski A W
CS Department of Chemistry, Warsaw University, Poland.
SO Polish journal of pharmacology and pharmacy, **(1987 Sep-Oct)** 39 (5) 585-96. Ref: 45
Journal code: 0366561. ISSN: 0301-0244.
CY Poland
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 198903
ED Entered STN: 19900306
Last Updated on STN: 19900306
Entered Medline: 19890327

AB In recent years several opioid receptors have been characterized (mu, kappa, delta, et cetera); furthermore, it has been suggested that different receptor types mediate different neurophysiological responses. It has also been found that there exist endogenous opioid **peptides** which reveal some selectivity for a particular receptor type. These observations created a need for selective agonists and antagonists of a particular receptor type, and indicated a possibility of developing selective opioid drugs with reduced side effects. All endogenous **peptides** have an identical N-terminal part, which suggests that opioid receptor pockets in the message part are similar or identical. The main elements which differentiate the selectivity of endogenous **peptides** are surroundings of receptor pockets, different organization of opioid receptors and their interactions with other receptors and enzymatic systems. This opens a possibility of successful modifications of biochemical and/or physiological properties of opioid **pharmacophores** through modification of the elements which could be connected with the opioid message. Depending on the character of the connecting element, the **pharmacophores** may be divided into three main types: (i) opioid **pharmacophores** coordinated with the address; (ii) bivalent opioids; (iii) bifunctional **pharmacophores**
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